APPENDIX OF PENDING CLAIMS

1. (Amended) A method of screening a human subject for an increased risk of developing a hereditary lymphedema, comprising the steps of:

(a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering the encoded amino acid sequence or expression of at least one VEGFR-3 allele; and

(b) screening for an increased risk of developing hereditary lymphedema from the presence or absence of said mutation, wherein the presence of a mutation altering the encoded amino acid sequence or expression of at least one VEGFR-3 allele in the nucleic acid correlates with an increased risk of developing hereditary lymphedema.

2. A method according to claim 1 wherein the assaying step comprises determining the presence or absence of a mutation altering a tyrosine kinase domain amino acid sequence of the protein encoded by the VEGFR-3 allele.

3. A method according to claim 1 wherein the assaying step comprises determining the presence or absence of a missense mutation in a VEGFR-3 allele at a position corresponding to one of codons 857, 1041, 1044 and 1049 of the VEGFR-3-encoding sequence set forth in SEQ ID NO: 1.

4. A method according to claim 1 wherein the assaying step comprises determining the presence or absence of a missense mutation in the VEGFR-3 allele at a position corresponding to codon 1114 of the VEGFR-3-encoding sequence set forth in SEQ ID NO: 1.

5. A method according to claim 1 wherein the assaying step comprises at least one procedure selected from the group consisting of:

(a) determining a nucleotide sequence of at least one codon of at least one VEGFR-3 allele of the human subject;

(b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences;

(c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and

(d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

6. A method according to claim 1 wherein the assaying step comprises: performing a polymerase chain reaction (PCR) to amplify nucleic acid comprising VEGFR-3 coding sequence, and determining nucleotide sequence of the amplified nucleic acid.

7. A method of screening for a VEGFR-3 hereditary lymphedema genotype in a human patient, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from said patient, said nucleic acid including sequences corresponding to said patient's VEGFR-3 alleles;

(b) analyzing said nucleic acid for the presence of a mutation or mutations;

(c) determining a VEGFR-3 genotype from said analyzing step; and

(d) correlating the presence of a mutation in a VEGFR-3 allele with a hereditary lymphedema genotype.

8. The method according to claim 7 wherein said biological sample is a cell sample.

9. The method according to claim 7 wherein said analyzing comprises sequencing a portion of said nucleic acid, said portion comprising at least one codon of said VEGFR-3 alleles.

10. The method according to claim 7 wherein said nucleic acid is DNA.

11. The method according to claim 7 wherein said nucleic acid is RNA.

14. An oligonucleotide useful as a probe for identifying polymorphisms in a human Flt4 receptor tyrosine kinase gene, the oligonucleotide comprising 6-50 nucleotides that have a sequence that is identical or exactly complementary to a portion of a wild type human VEGFR-3 gene sequence or VEGFR-3 coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution.

15. An oligonucleotide according to claim 14 wherein the nucleotide sequence is exactly identical or exactly complementary to a portion of the human VEGFR-3 coding sequence set forth in SEQ ID NO: 1, except for a nucleotide substitution at a position corresponding to a nucleotide selected from the group consisting of bases 2546 through 2848 and bases 3044 through 3514.

16. An oligonucleotide according to claim 14 wherein the nucleotide sequence is exactly identical or exactly complementary to a portion of the human VEGFR-3 coding sequence set forth in SEQ ID NO: 1, except for a nucleotide substitution at a position corresponding to nucleotide 3360 of SEQ ID NO: 1.

17. An oligonucleotide according to claim 14 wherein the nucleotide sequence is exactly identical or exactly complementary to a portion of the human VEGFR-3 coding sequence set forth in SEQ ID NO: 1, except for a nucleotide substitution at a position corresponding to a nucleotide selected from the group consisting of position 2588, position 3141, position 3150 and position 3164 of SEQ ID NO: 1.

18. A kit comprising at least two oligonucleotides of the formula X_nYZ_m or its complement;

where n and m are integers from 0 to 49;

where $5 \leq (n + m) \leq 49$;

where X_n is a stretch of n nucleotides identical to a first portion of SEQ ID NO: 1, said first portion ending immediately upstream (5') of position 3360 of SEQ ID NO: 1; and

where Z_m is a stretch of m nucleotides identical to a second portion of SEQ ID NO: 1, said second portion beginning immediately downstream (3') of position 3360 of SEQ ID NO: 1; and

wherein Y represents a nucleotide selected from the group consisting of adenine, guanine, cytosine, thymine, and uracil nucleotides.

19. A kit comprising at least two oligonucleotides of the formula X_nYZ_m or its complement;

where n and m are integers from 0 to 49;

where $5 \leq (n + m) \leq 49$;

where X_n is a stretch of n nucleotides identical to a first portion of SEQ ID NO: 1, said first portion ending immediately upstream (5') of position W of SEQ ID NO: 1; and

where Z_m is a stretch of m nucleotides identical to a second portion of SEQ ID NO: 1, said second portion beginning immediately downstream (3') of position W of SEQ ID NO: 1;

wherein position W of SEQ ID NO: 1 is selected from the group consisting of nucleotides 2588, 3141, 3150, and 3164 of SEQ ID NO: 1; and

wherein Y represents a nucleotide selected from the group consisting of adenine, guanine, cytosine, thymine, and uracil nucleotides.

20. An array of oligonucleotide probes immobilized on a solid support, wherein each probe occupies a separate known site in the array; and wherein the array includes at least one probe set comprising two to four probes, wherein one probe is exactly identical or exactly complementary to a wild type human VEGFR-3 coding sequence, and the other one to three members of the set are exactly identical to the first member, but for at least one different nucleotide, which different nucleotide is located in the same position in each of the one to three additional set members.

21. An array of oligonucleotide probes immobilized on a solid support according to claim 20, wherein each probe occupies a separate known site in the array; and wherein the array includes at least one probe set comprising two to four probes, wherein one probe is exactly identical or exactly complementary to a portion of a human VEGFR-3 coding sequence set forth in SEQ ID NO: 1, and the other one to three members of the set are exactly identical to the first member, but for at least one different nucleotide, which different nucleotide is located in the same position in each of the one to three additional set members, said position corresponding to a position selected from the group consisting of bases 2546 through 2848 and bases 3044 through 3514 of SEQ ID NO: 1.

22. A purified polynucleotide comprising a nucleotide sequence encoding a human VEGFR-3 protein variant, wherein said polynucleotide is capable of hybridizing to the complement of SEQ ID NO: 1 under the following hybridization conditions:

hybridization at 42°C in 50% formamide, 5X SSC, 20 mM $Na•PO_4$, pH 6.8; and

washing in 0.2X SSC at 55°C;

and wherein the encoded VEGFR-3 protein variant has an amino acid sequence that differs from the amino acid sequence set forth in SEQ ID NO: 2 at one or more positions selected from the group consisting of amino acids 843 to 943 of SEQ ID NO: 2 and amino acids 1009 to 1165 of SEQ ID NO: 2.